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Adverse outcomes in the foetus with use of inhaled corticosteroids during pregnancy: systematic review and meta-analysis

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Objectives: Inhaled corticosteroids (ICS) are widely recommended in patients with asthma but it is unclear whether there are significant adverse effects when used in pregnancy. We aimed to conduct a systematic review of adverse outcomes with long-term ICS use in pregnancy.

Methods: We initially searched MEDLINE and EMBASE in July 2013, and subsequently updated the search to May 2016 using PubMed. We selected randomized trials and controlled observational studies of any ICS compared to non-ICS use in pregnant women with asthma. The outcomes of interest were congenital malformations, birth weight, low birth weight (< 2500 grams), and intrauterine growth restriction or small for gestational age. We used RevMan 5.3.5 to perform random effects meta-analysis of adjusted odds ratio (aOR) or mean difference of continuous outcomes, and we assessed heterogeneity using the I^2 statistic.

Results: We screened 2108 titles and abstracts and finally included 15 relevant studies in the systematic review. Overall, a total of more than 140 000 participants were enrolled in these 15 studies, which were conducted in the US, Canada, United Kingdom, Australia, Denmark, Sweden and Australia. These included two randomized controlled trials, whereas the remaining studies were all observational in nature. For congenital malformations, pooled aOR of ICS use from four observational studies was 1.03 (95% CI 0.97-1.10, I^2 =5%). The mean birthweight was marginally reduced in ICS users as compared to non-users, -76 grams (95% CI -150.6 to -2.0 grams, I^2 =19%), which should be interpreted in context of typical birthweights of >3000 grams. In our meta-analysis, we did not detect any significant elevation in the odds of low birthweight, small for gestational age, or intrauterine growth restriction in association with ICS use. Limitations of the studies include lack of power to detect rare events, and the threat of residual confounding, particularly with inadequate adjustment for asthma severity. Selective outcome reporting and publication bias are a possibility, whereby non-significant results were not fully reported and therefore could not be included in the meta-analysis.

Conclusion: The available evidence does not suggest that ICS use was associated with major harm effects on the foetus. Any adverse effects from ICS use should be balanced against the potential benefits of better asthma control for the mother and the foetus.